# **IEDB** Tools

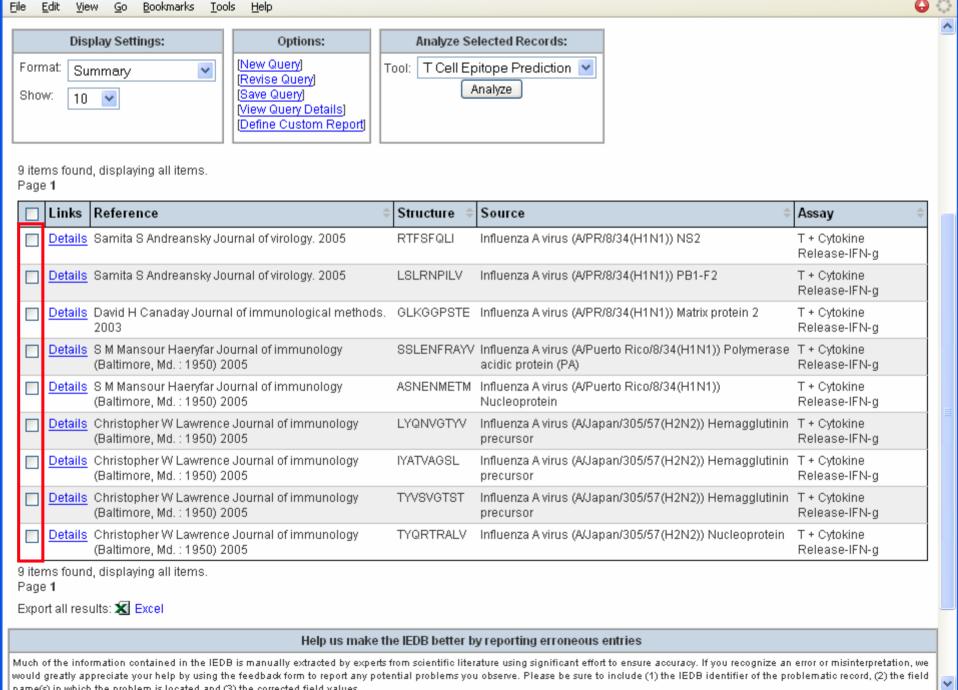
BRC Meeting February 6, 2006



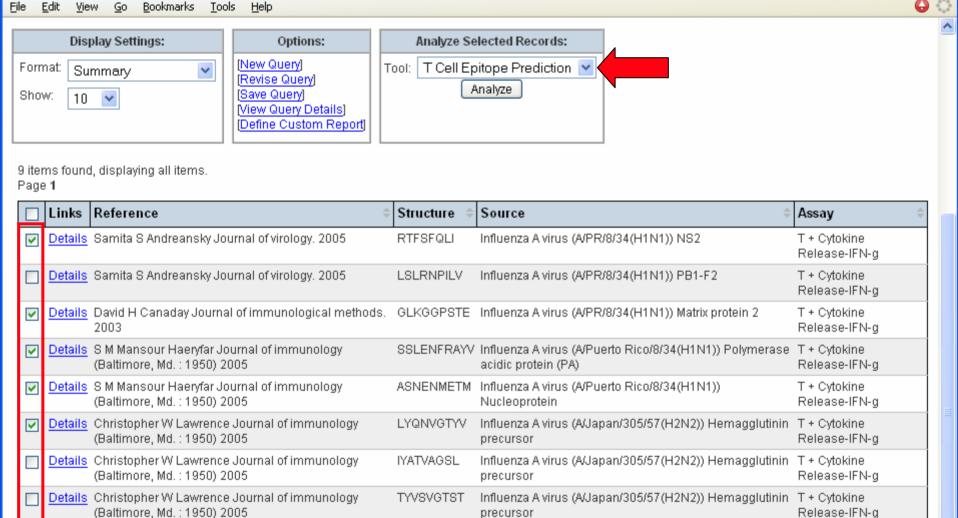
## **Outline**

- Tool integration
  - T cell epitope identification tools
  - B cell epitope identification tools
  - Epitope analysis tools
  - Visualization tools





🐸 Immune Epitope Database and Analysis Resource - Mozilla Firefox



9 items found, displaying all items.

Details Christopher W Lawrence Journal of immunology

(Baltimore, Md.: 1950) 2005

🐸 Immune Epitope Database and Analysis Resource - Mozilla Firefox

Page 1

Export all results: X Excel

## Help us make the IEDB better by reporting erroneous entries

Much of the information contained in the IEDB is manually extracted by experts from scientific literature using significant effort to ensure accuracy. If you recognize an error or misinterpretation, we would greatly appreciate your help by using the feedback form to report any potential problems you observe. Please be sure to include (1) the IEDB identifier of the problematic record, (2) the field name(s) in which the problem is located and (2) the corrected field values.

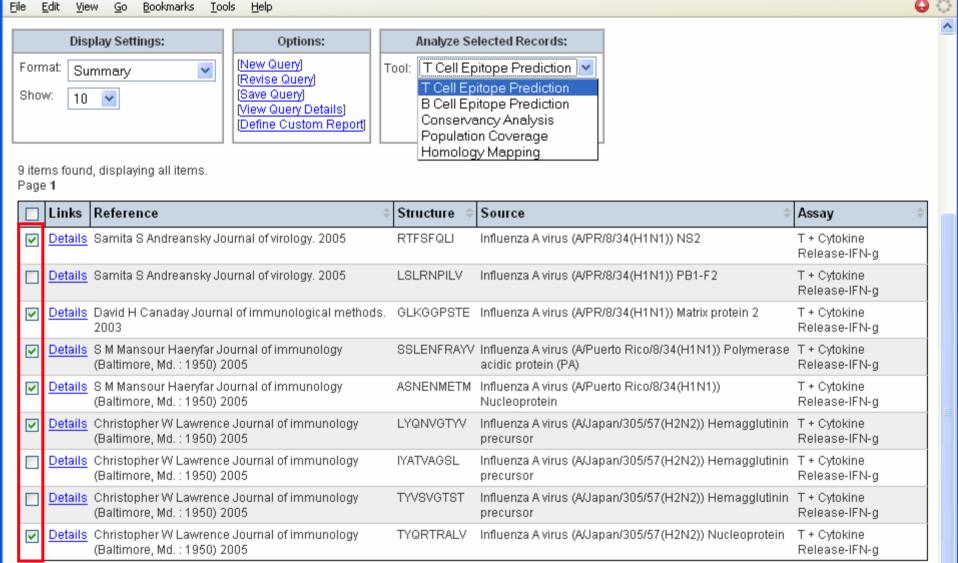
TYQRTRALV

precursor

Influenza A virus (A/Japan/305/57(H2N2)) Nucleoprotein

T + Cytokine

Release-IFN-a



Page 1

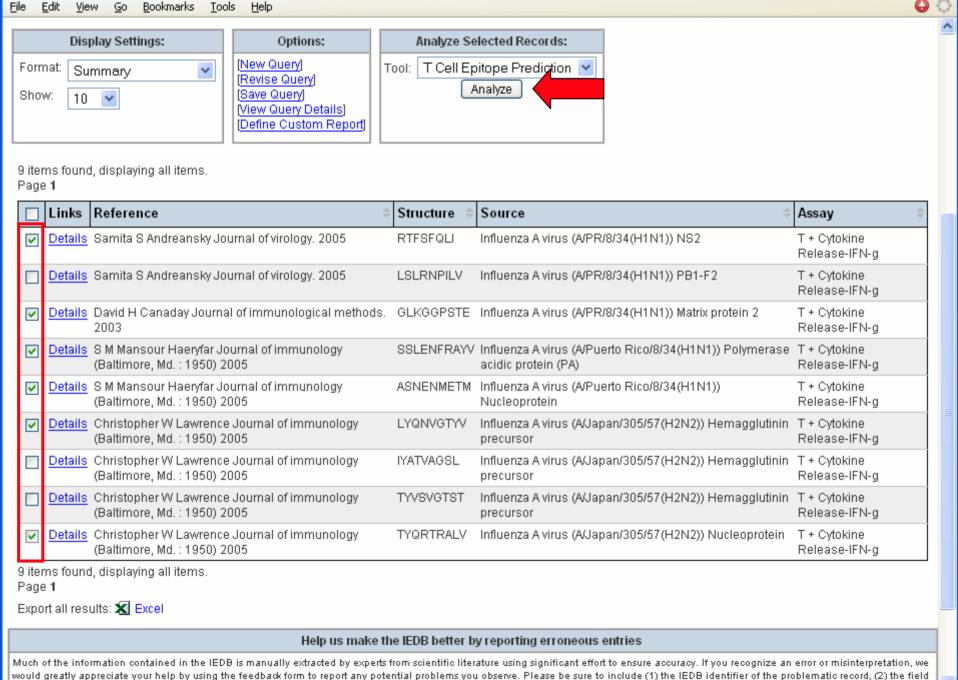
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#### T-Cell Epitope Identification

This is an intermediate page used for validating your previously selected query results data. Selections that are invalid because they are missing data necessary for tool execution are indicated with a red border

	<ul><li>Epitope</li></ul>	Source Protein
V	RTFSFQLI	NS2
V	GLKGGPSTE	Matrix protein 2
V	SSLENFRAYV	Polymerase acidic protein (PA)
V	ASNENMETM	Nucleoprotein
>	LYQNVGTYV	Hemagglutinin precursor
~	TYQRTRALV	Nucleoprotein

MHC class I binding prediction Send to Tool

The T cell epitope identification tools implement a number of methods to scan a set of amino acid sequences for peptides that are potential T cell epitopes. Use the radio buttons in the header row of the table to specify if sequences of epitopes or their source proteins should be scanned. Use the checkboxes on the left to select which rows this applies to. The list box below the table selects if the sequences will be scanned using predictions of peptide binding to MHC alone or including two additional processing steps: proteasomal cleavage and TAP transport. When selecting predictions for protein sequences, please allow some time for their retrieval from GenBank.



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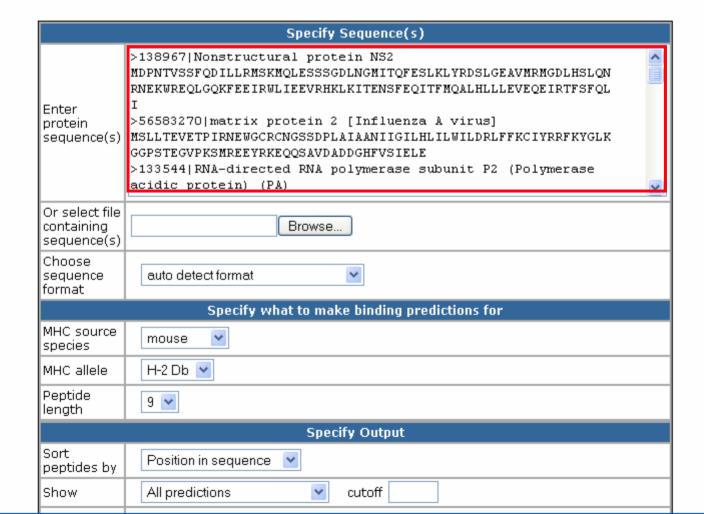
MHC class I binding prediction

T MHC class I processing prediction that a number of methods to scan a set of the MHC class II binding prediction that are potential T cell epitopes. Use the radio buttons in the header row of the table to specify if sequences of epitopes or their source proteins should be scanned. Use the checkboxes on the left to select which rows this applies to. The list box below the table selects if the sequences will be scanned using predictions of peptide binding to MHC alone or including two additional processing steps: proteasomal cleavage and TAP transport. When selecting predictions for protein sequences, please allow some time for their retrieval from GenBank.



## MHC-I binding predictions

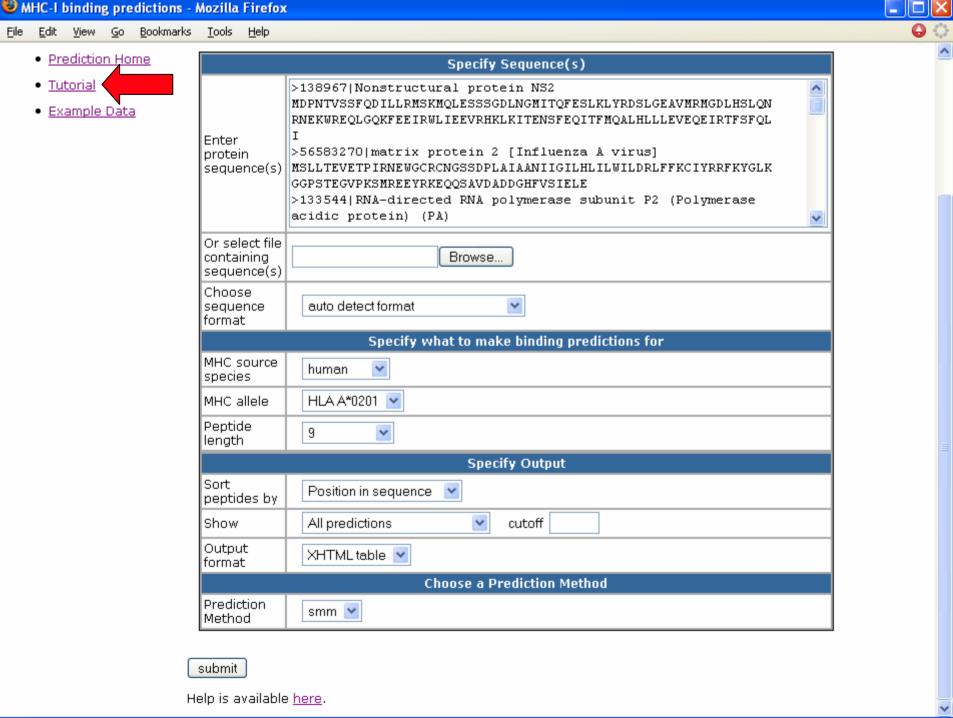
- Prediction Home
- <u>Tutorial</u>
- Example Data



# **Outline**

- Tool integration
- T cell epitope identification tools
  - B cell epitope identification tools
  - Epitope analysis tools
  - Visualization tools





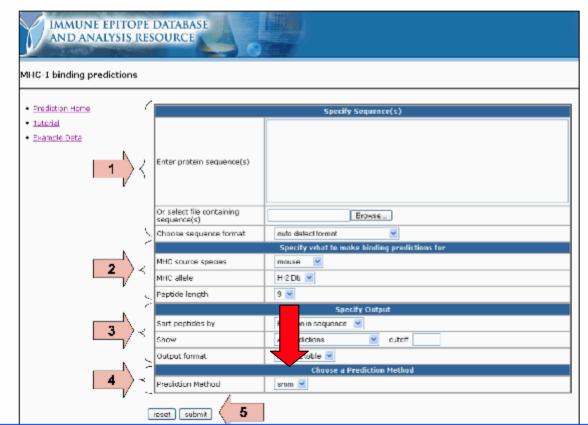


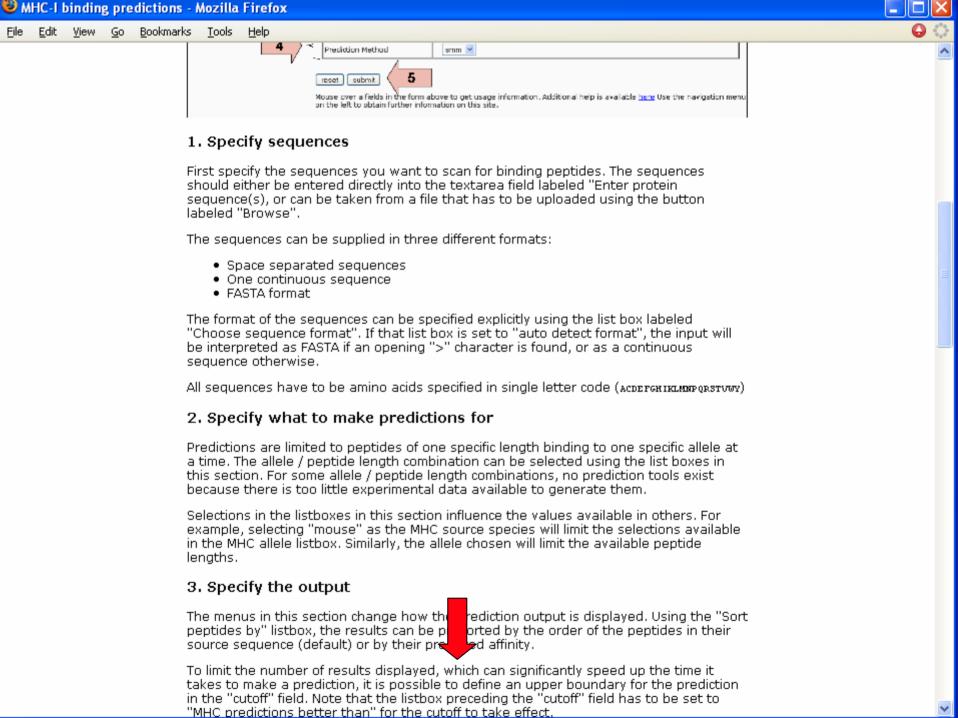
## MHC-I binding predictions - Tutorial

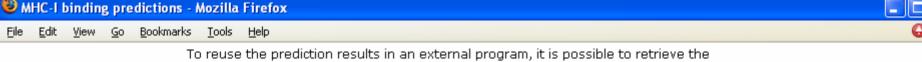
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## How to obtain predictions

This website provides access to predictions of peptide binding to MHC class I molecules. The screenshot below illustrates the steps necessary to make a prediction. Each of the steps is described in more detail below.







predictions in a plain text format. To do this, choose "Text file" in the output format listbox.

## 4. Choose a prediction method

The prediction method list box allows choosing between three currently implemented MHC class I binding prediction methods:

- Artificial neural network (ann)
- Average relative binding (arb)
- Stabilized matrix method (smm)

Please note that changing the prediction method can influence what allele / peptide length combinations are available in section 2. For example, the neural network prediction is currently limited to peptides of length 9.

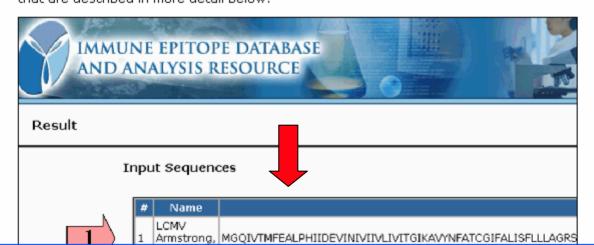
The IEDB team is in the process of making a formalized comparison of the performance of the three methods. Until that is completed, no guidance can be given as to which method should be chosen.

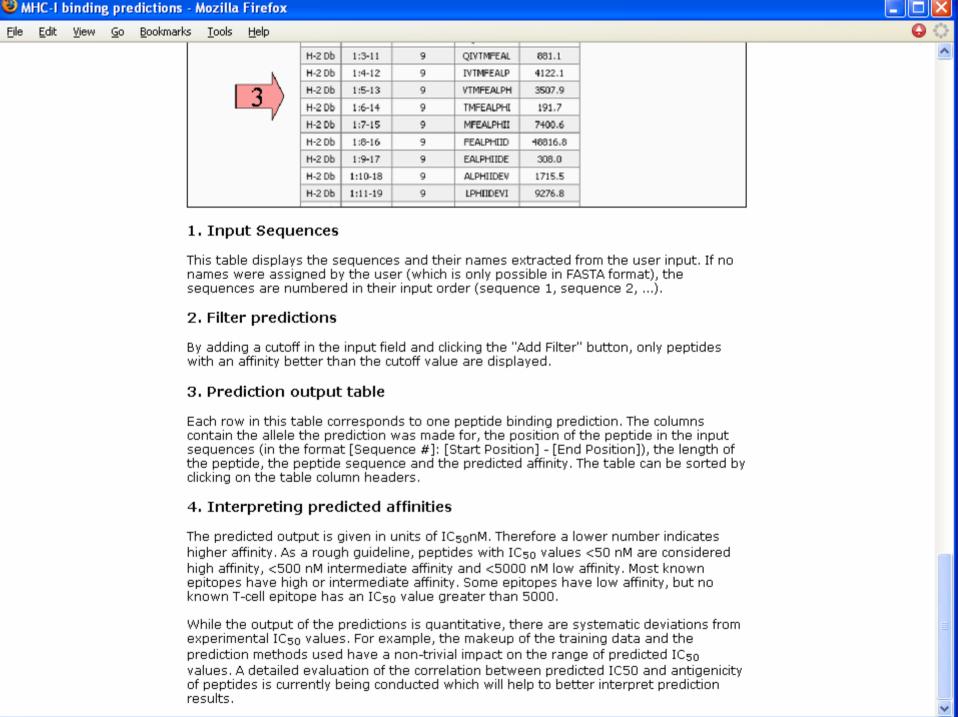
#### 5. Submit the prediction

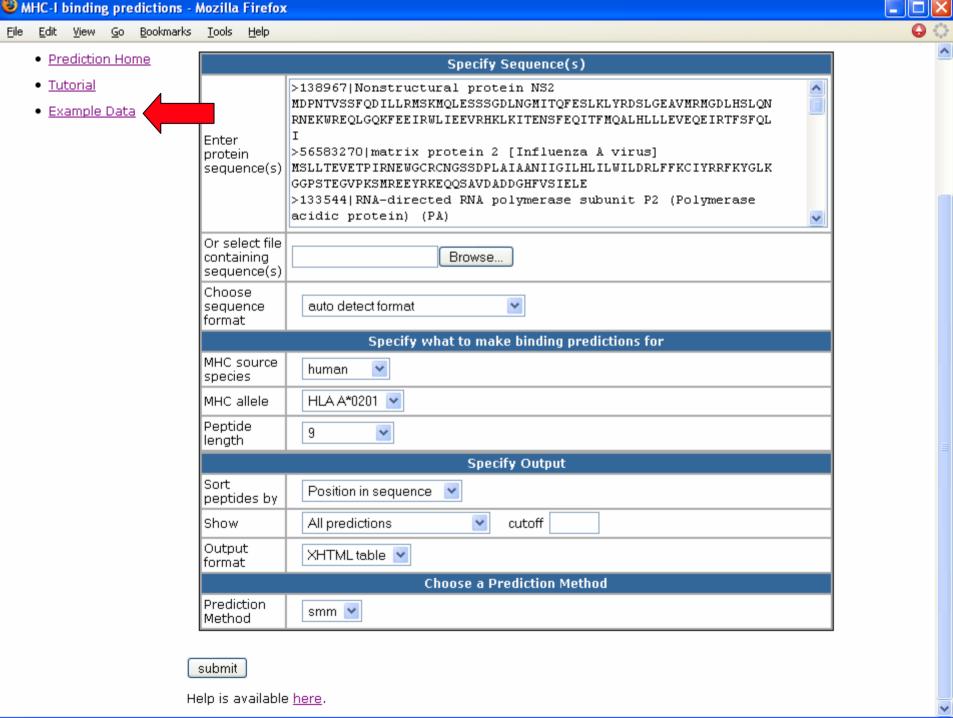
This one is easy. Click the submit button, and a result screen similar to the one below should appear.

## Interpreting prediction output

Below is a screenshot of a prediction output page, with four relevant sections marked that are described in more detail below.









#### MHC-I binding predictions - Example data

- · Prediction Home
- Tutorial
- Example Data

Choose one of the radio buttons below to select protein sequence(s) containing MHC class I epitopes described in the literature with defined MHC restrictions for which predictions are available. These sequences will be transfered to the MHC class I binding predictions when clicking the "Submit" button. These test-datasets are meant to demonstrate the functionality of the tools and are by no means considered equivalent to a formal performance evaluation.

GP and NP protein of LCMV virus strain armstrong

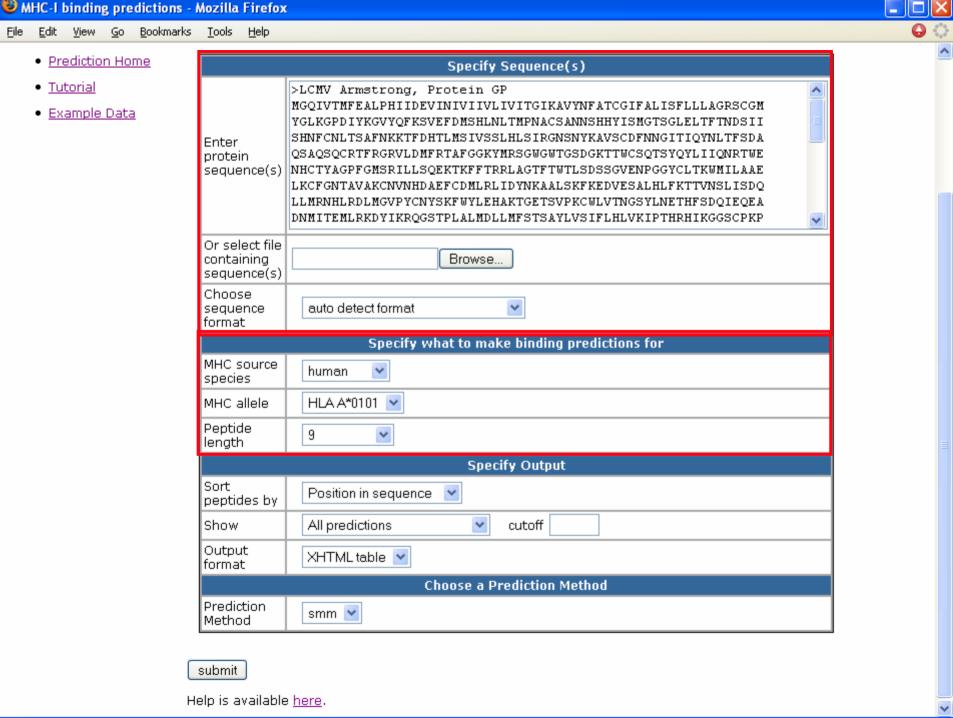
Peptide	Length	MHC restriction
FQPQNGQFI	9	H-2 Db
KAVYNFATC	9	H-2 Db
ISHNFCNL	8	H-2 Kb
YTVKYPNL	8	H-2 Kb

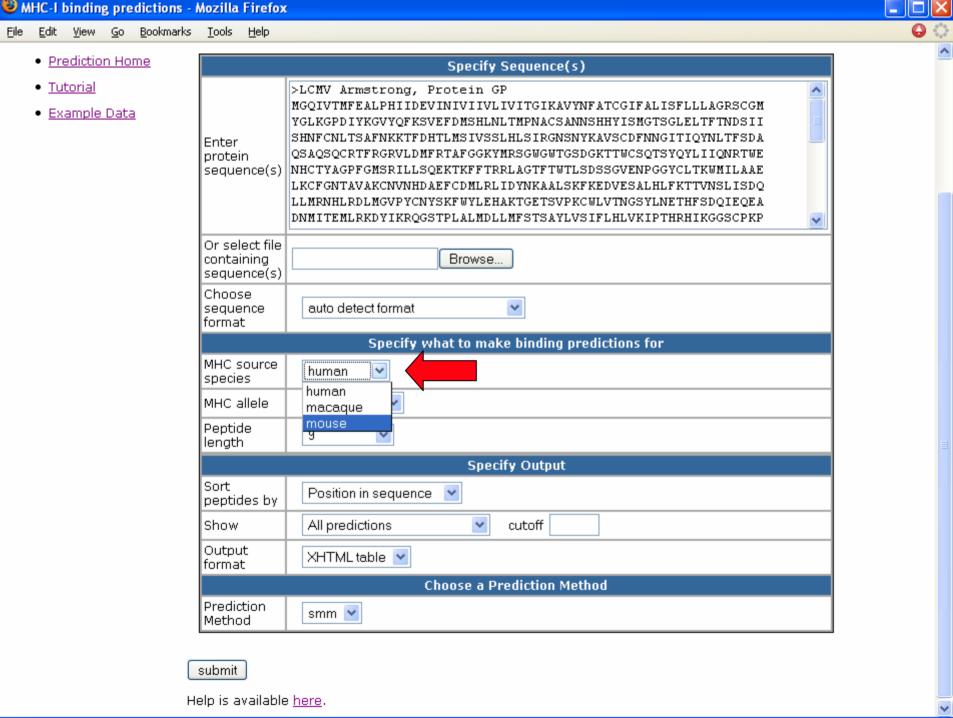
O SARS spike protein

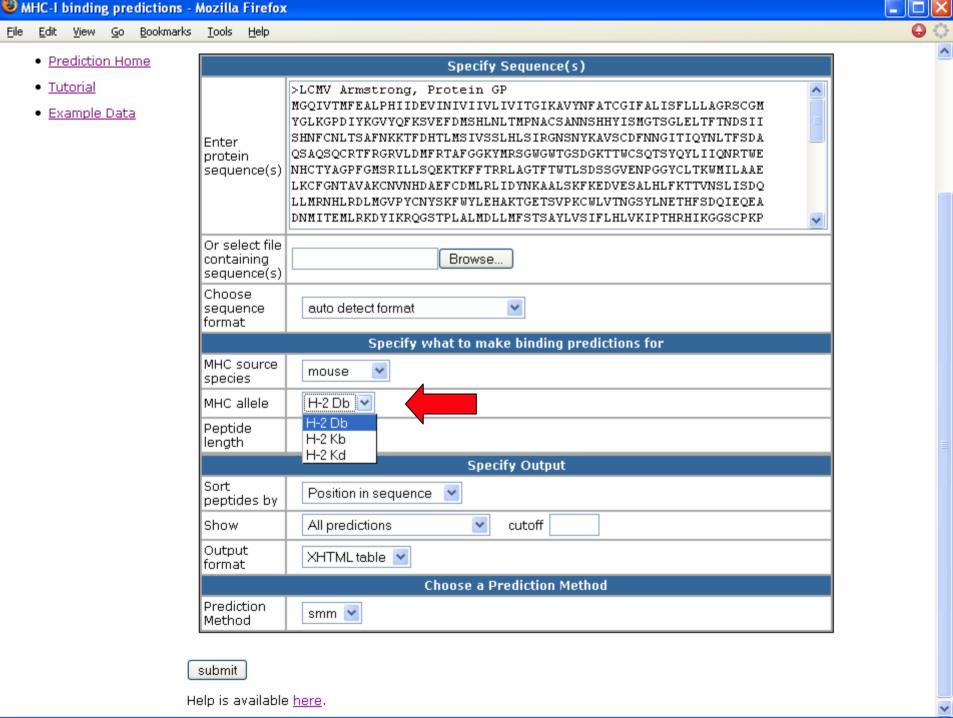
Peptide	Length	MHC restriction	
FIAGLIAIV	9	HLA A*0201	
LITGRLQSL	9	HLA A*0201	
RLNEVAKNL	9	HLA A*0201	

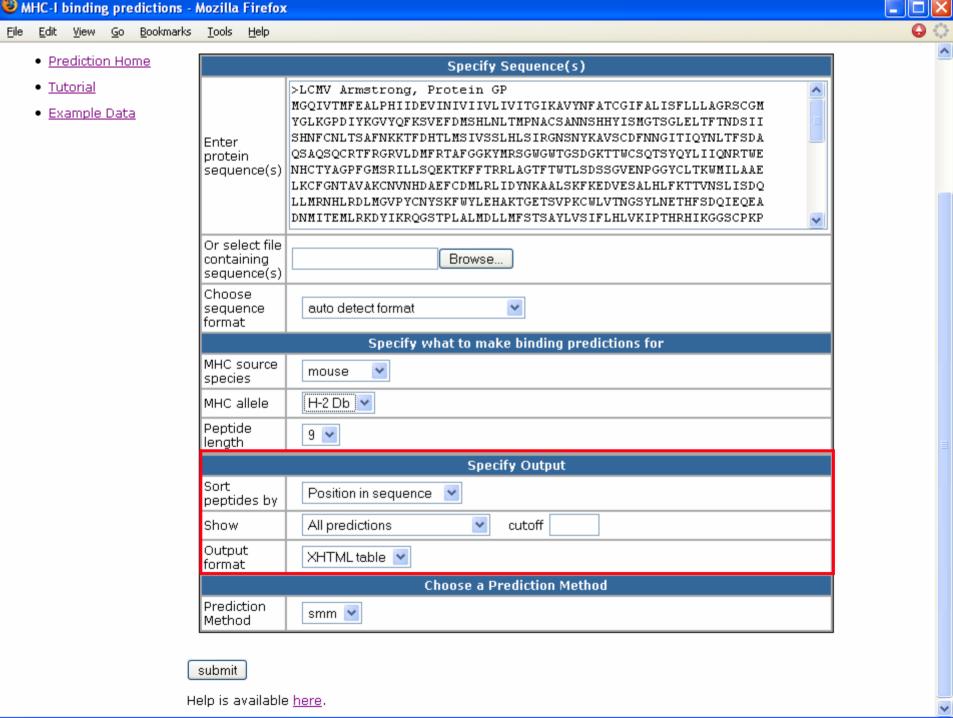


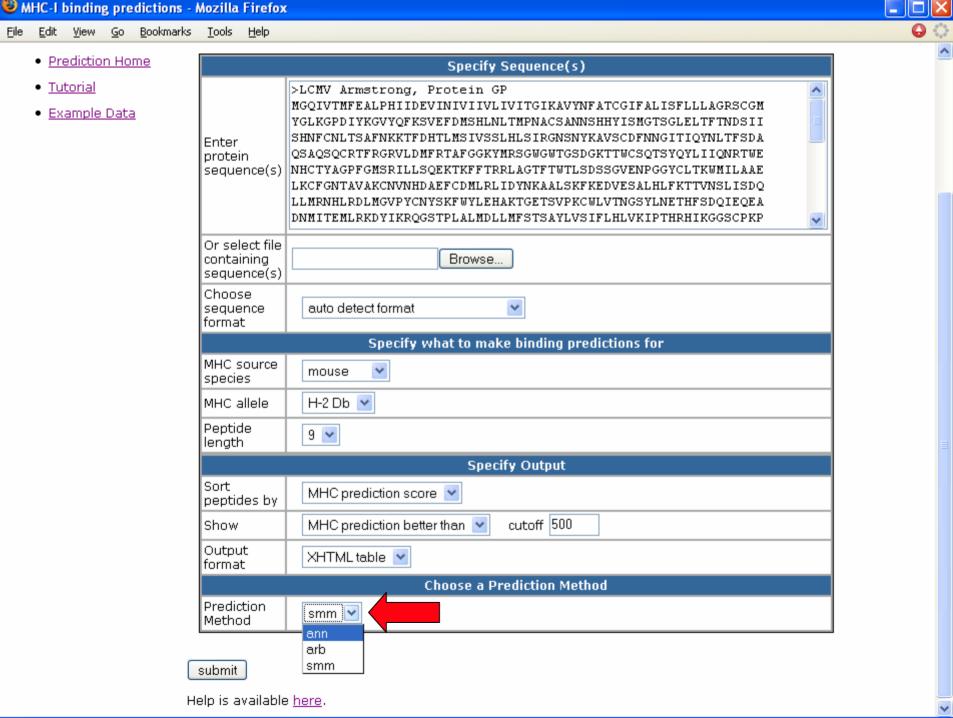
You can also use these sequences with MHC class I processing predictions

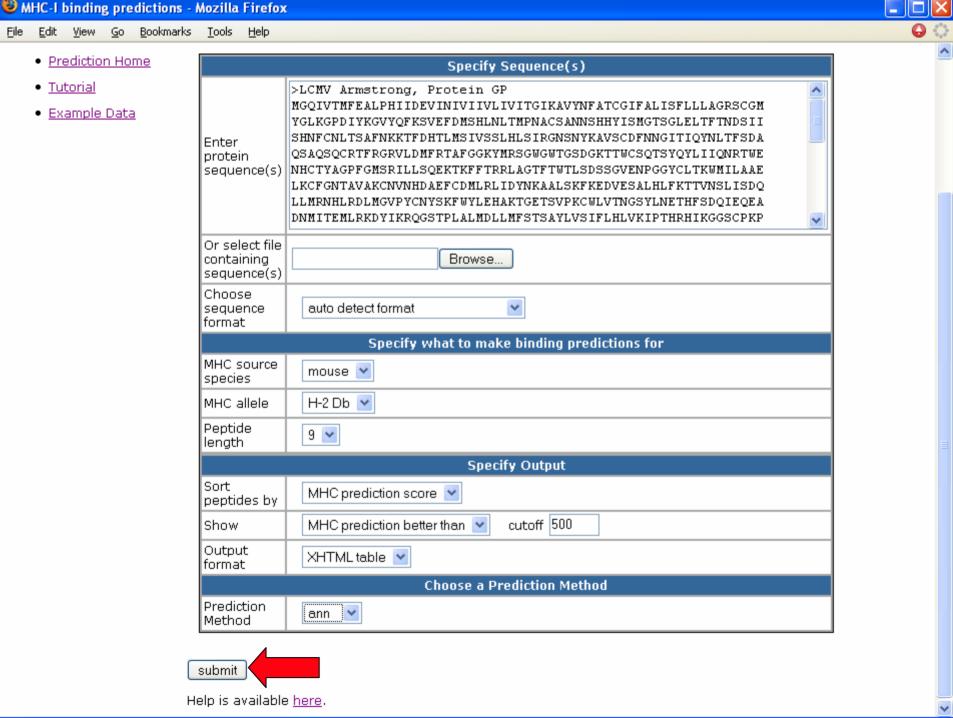


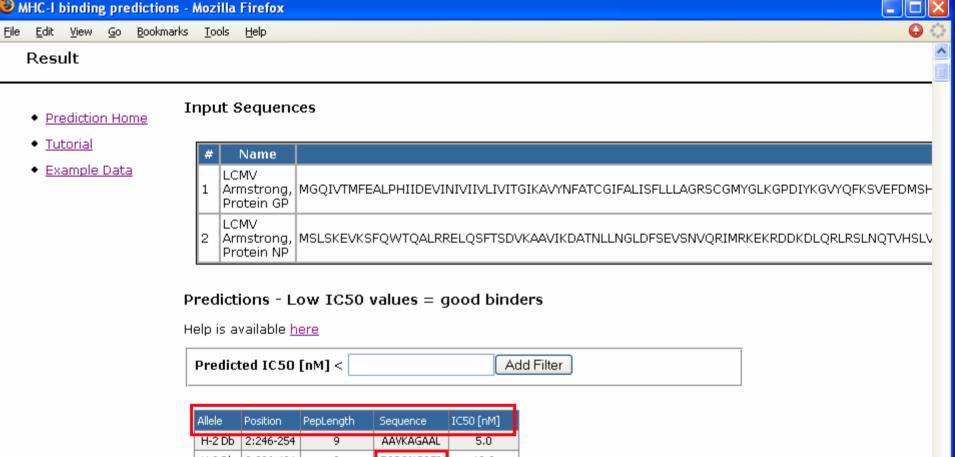












Allele	Position	PepLength	Sequence	IC50 [nM]
H-2 Db	2:246-254	9	AAVKAGAAL	5.0
H-2 Db	2:396-404	9	FQPQNGQFI	13.0
H-2 Db	1:353-361	9	DQLLMRNHL	17.9
H-2 Db	2:252-260	9	AALLDGGNM	20.8
H-2 Db	2:29-37	9	AAVIKDATN	22.2
H-2 Db	2:339-347	9	PAVNSPRPA	26.3
H-2 Db	1:434-442	9	LALMDLLMF	36.8
H-2 Db	1:33-41	9	KAVYNFATC	39.0
H-2 Db	1:38-46	9	FATCGIFAL	43.0
H-2 Db	1:44-52	9	FALISFLLL	43.0
H-2 Db	1:93-101	9	SANNSHHYI	43.9
H-2 Db	2:376-384	9	NAPTWIDIE	45.2
H-2 Db	2:276-284	9	KAVLGAKRK	45.6





# T cell epitope identification

- More tools:
  - MHC class I processing predictions (Proteasome / TAP / MHC)
  - MHC class II binding predictions
- Ongoing evaluation
  - transparent process
  - public datasets
- Machine interface



## **Outline**

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# Scope

- Types of antibody epitope
  - Continuous
  - Discontinuous
- Aim of 1<sup>st</sup> release:
  - Implementation of methods for predicting continuous antibody epitope from protein sequences



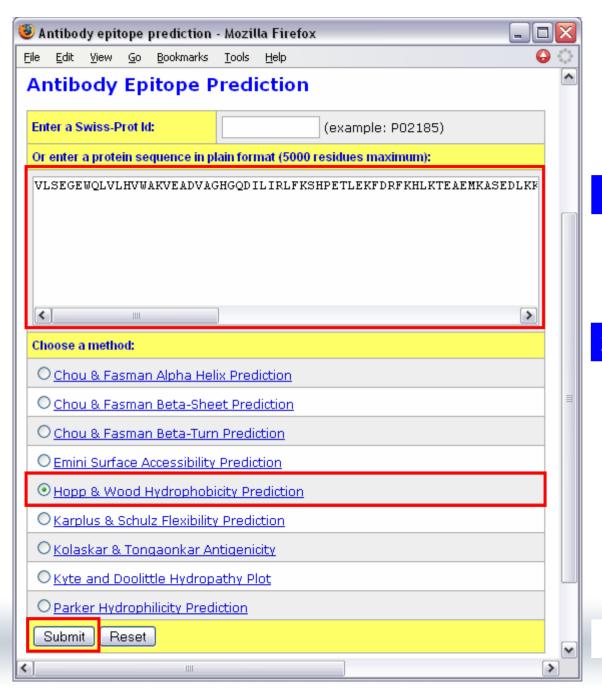
## **General Basis**

- Locations of continuous epitopes within protein sequences have been correlated with different parameters such as:
  - Hydrophilicity
  - Flexibility
  - Accessibility
  - Turns
  - Exposed surface
  - Polarity
  - Antigenic propensity
  - ...
- This has led to a search for empirical rules that would allow the position of continuous epitopes to be predicted from certain features of the protein sequence.

# Implemented Methods

- Hyrophobicity/hydrophilicity
  - Hopp and Wood hydrophobicity prediction
  - Parker hydrophilicity prediction
  - Kyte and Doolittle hydropathy plot
- Secondary structure
  - Chou & Fasman alpha helix prediction
  - Chou & Fasman beta-sheet prediction
  - Chou & Fasman beta-turn prediction
- Flexibility
  - Karplus & Schulz flexibility prediction
    - 3 separate scales
- Surface exposure
  - Emini surface accessibility prediction
    - Emini equation
- Antigenicity
  - Kolaskar & Tongaonkar antigenicity prediction
    - Kolaskar prediction method

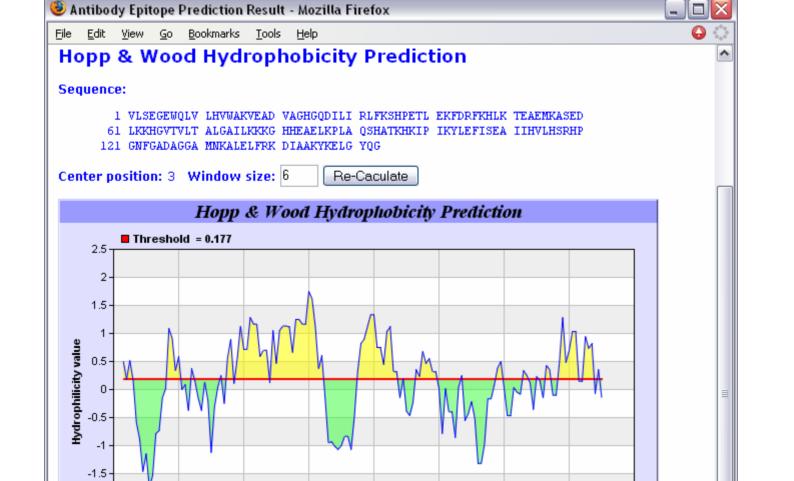




1. Specify protein sequence

2. Select a method





100

120

140

160



60

Click here to view plotted values in table format

40

20

-2

-2.5

Reference: Hopp TP & Woods KR. Prediction of protein antigenic determinants from amino acid sequences. Proc Natl Acad Sci U S A. 1981 Jun;78(6):3824-8.

80

Sequence Position



IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

# B-cell epitope identification

- Tool evaluation
  - B-cell epitope prediction workshop
- New tool development (2<sup>nd</sup> release)
  - Sequence-based approach
    - Linear epitopes
  - Structure-based approach
    - Linear + conformational epitopes



# **Outline**

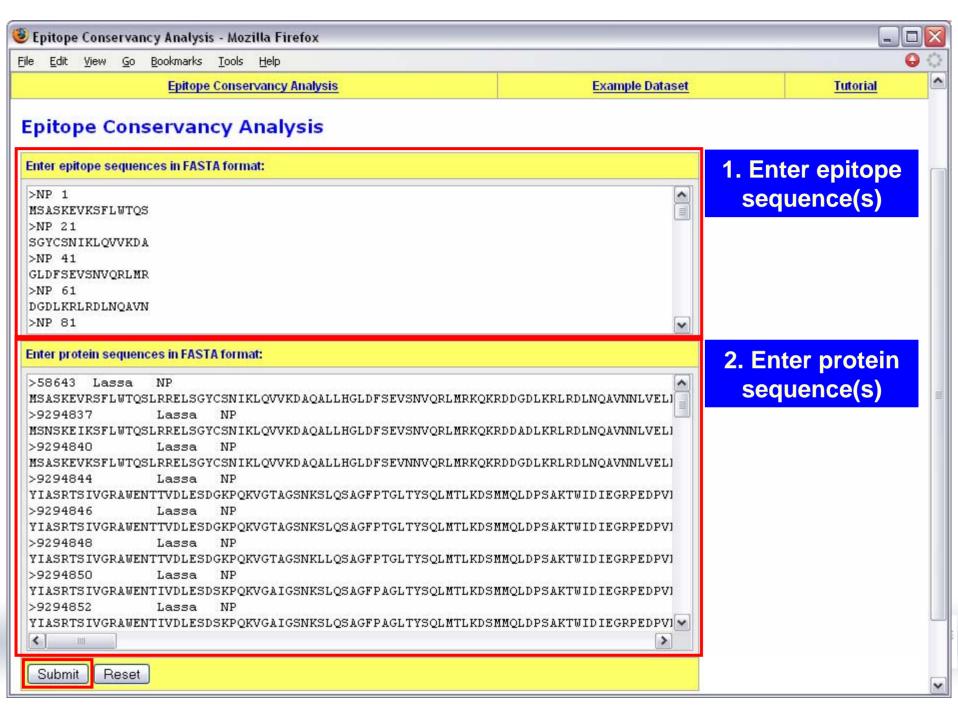
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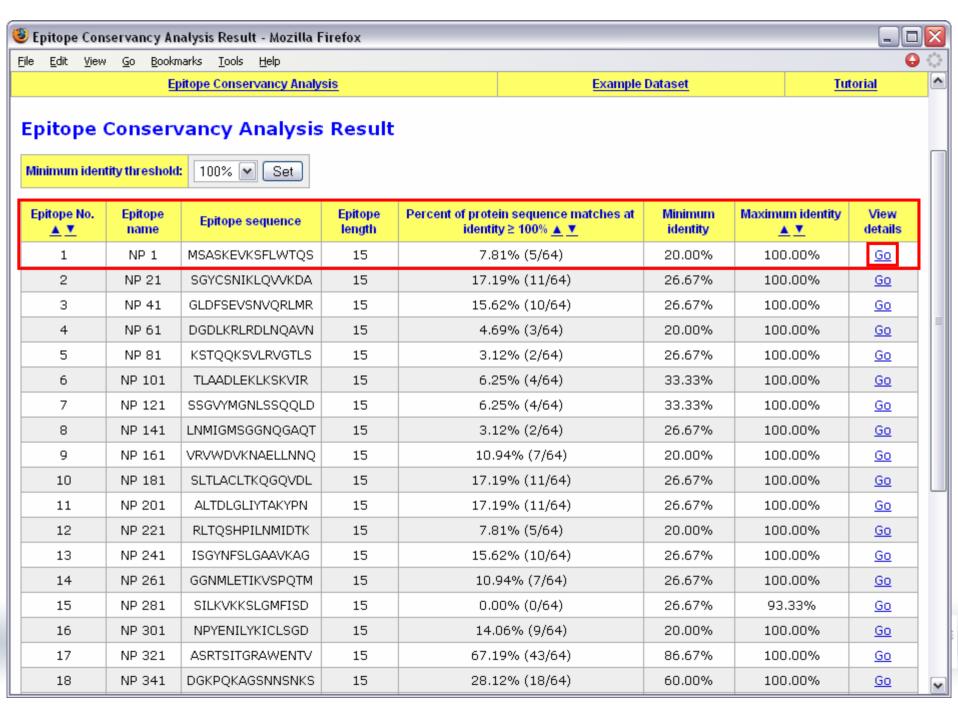


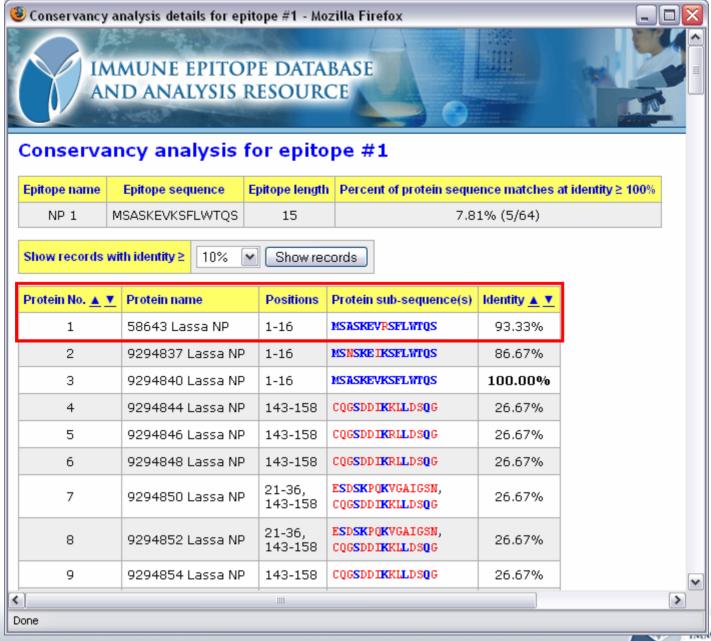
# Epitope Analysis I: Conservancy

How well is an epitope conserved across different sources (e.g. viral strains)?









Blue: Matching residues

Red: Non-matching residues



# Epitope Analysis II: Population Coverage

Given a set of epitopes with known MHC restriction(s), what is the predicted coverage in a population with known MHC allele frequencies?



# Background

#### MHC restriction

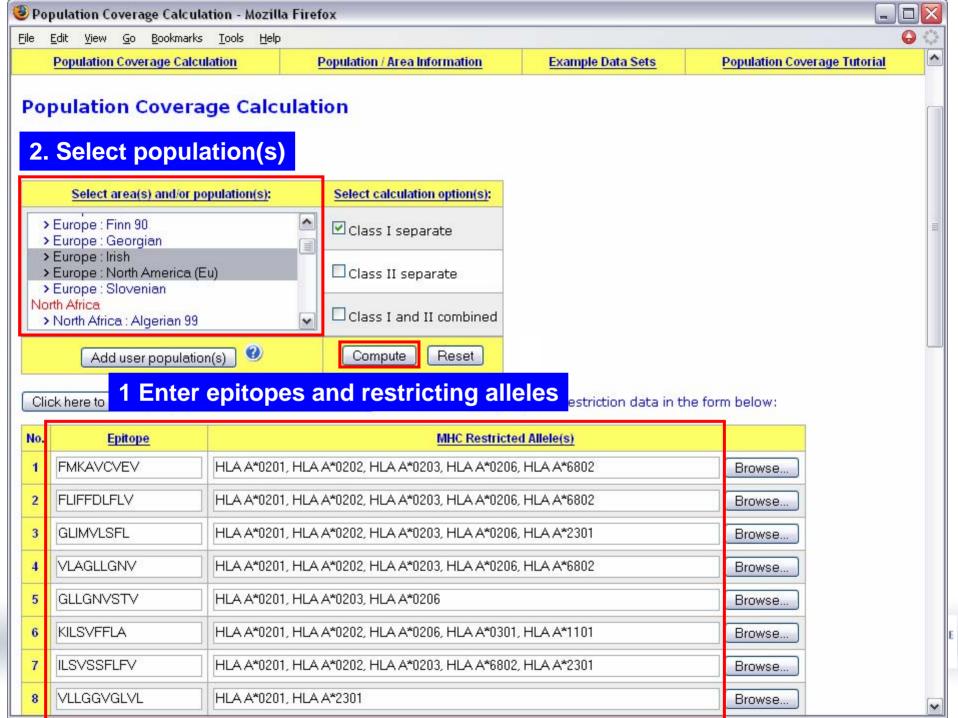
 T cell epitope will elicit a response only in individuals that express an MHC molecule capable of binding that particular epitope

### MHC polymorphism

- Over a thousand different MHC alleles are known in humans
- MHC alleles are found at dramatically different frequencies in different ethnicities

#### Motivation

 How to design T-cell epitope-based diagnostics and vaccines to be effective across different populations





	Class I				
Population / Area	Coverage <sup>a</sup>	Average hit <sup>b</sup>	PC90°		
Europe : Irish	97.77%	10.63	4.81		
Europe: North America (Eu)	96.37%	10.36	4.55		
Average (Standard deviation)	97.07% (0.70%)	10.49 (0.14)	4.68 (0.13)		

projected population coverage

**Coverage:** Projected population coverage

Average hit: Average number of epitope hits / HLA combinations recognized in the

population

PC90: Minimum number of epitope hits / HLA combinations recognized by 90% of the population

 $<sup>^{</sup>f b}$  average number of epitope hits / HLA combinations recognized by the population

<sup>•</sup> minimum number of epitope hits / HLA combinations recognized by 90% of the population

# **Outline**

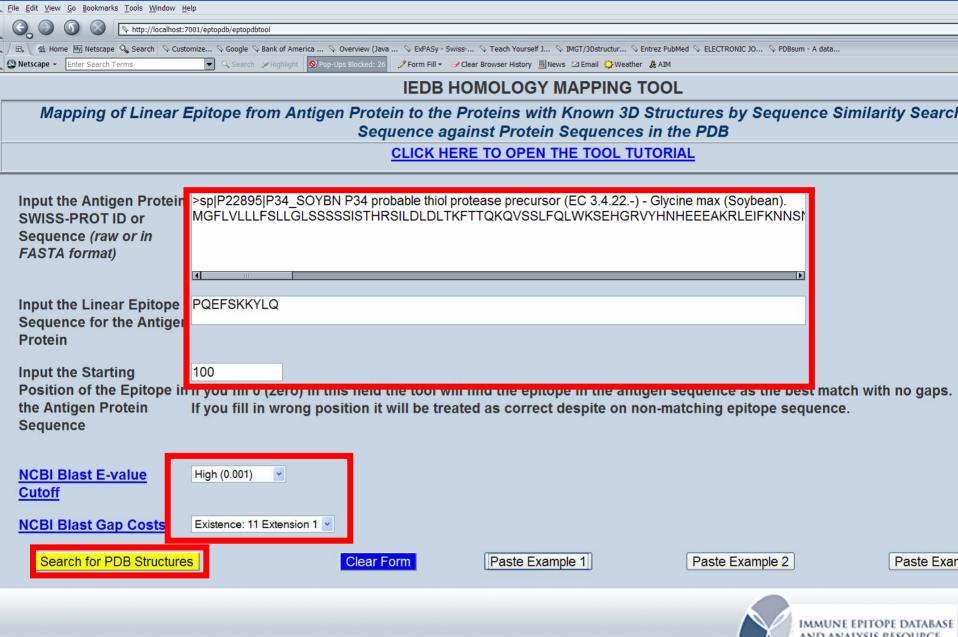
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# Visualization Tools

- Epitope Viewer
   Displays 3D structure and contact information curated in the IEDB
- Homology Mapping Tool Maps linear epitopes to proteins with known 3D structure from the Protein Data Bank (PDB)







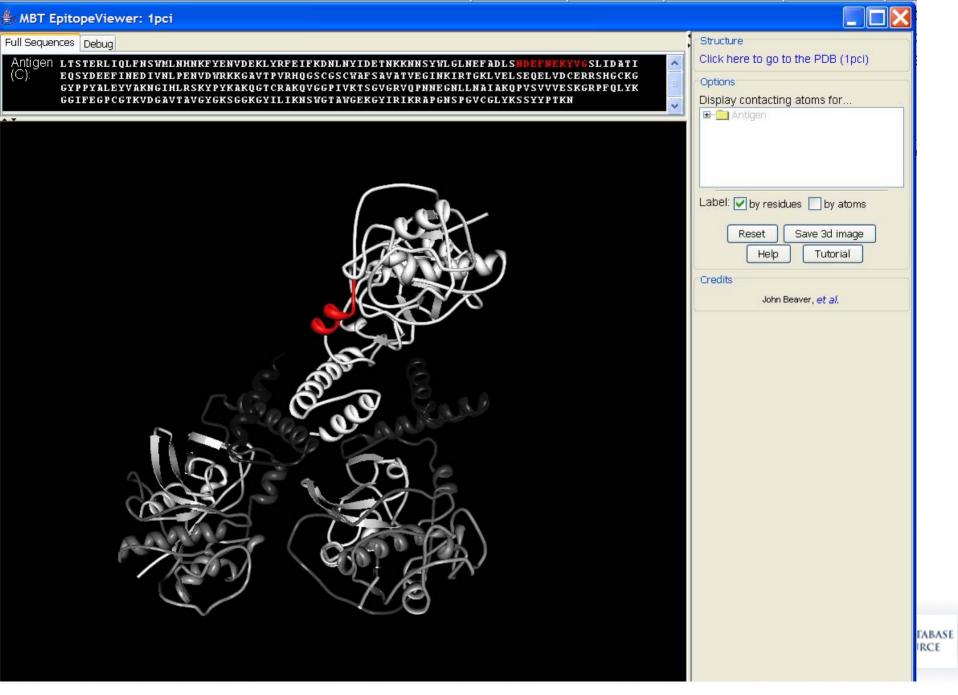
🐸 IEDB Homology Mapping Tool - Netscape

ID	Citati	Aligilileit	Length (including gaps)	Identity in the Alignment (including gaps) (%)	E value	Gaps in the Alignment	Epitope Sequence Identity in the Alignment	
1PCI	С	QUERY 35 TTQKQVSSLFQLWKSEHGRVYHNHEEEAKRLEIFKNNSNYIRDMNANRKSPHSHRLGLN * ** * * * * * * ***** * * * * ***** 1PCI_C 13 TSTERLIQLFNSWMLNHNKFYENVDEKLYRFEIFKDNLNYIDETNKKNNSYWLGLN	325	37.0	6.60854e-50	18	40.0 (4/10)	
	* *	ITPQEFSKKYLQAPKDVSQQIKMANI ++ ++ * LSNDEFNEKYVGSLIDATIEQSYDEI	Display in Epitope Viewer					
		QUERY 215 IATDDDYPYRAKEGRCKANKIQDKVTIDGYETLIMSDESTESETEQAFLSAILEQPISV.  * *** ** * * * * * * * * * * * * * *						
1PCI	В	QUERY 35 TTQKQVSSLFQLWKSEHGRVYHNHEEEAKRLEIFKNNSNYIRDMNANRKSPHSHRLGLNK  * * * * * * * * * * * * * * * * * * *	325	37.0	6.60854e-50	18	40.0 (4/10)	
						MMUNE EPITO	OPE DATABASE	



E Value Number of

Query



# Acknowledgments

- LIAI
  - A. Sette
  - H. Bui
  - J. Mokili
  - S. Wilson
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  - J. Sidney
  - N. Salimi
  - G. Moore
  - L. Zerebsky
  - R. Chen
  - R. Vita
  - M. Alexander
- SAIC
  - S. Stewart
  - D. di Ferdinando
  - P. Surko
  - S. Way
  - T. Carolan

- SDSC
  - P. Bourne
  - J. Pomarenko
  - J. Beaver
  - K. Addess
- NIAID
- OTHERS
  - V. Brusic
  - W. Hildebrand
  - S. Buus
  - Large Scale Epitope Groups
  - Immunological Databases



- Assigning source proteins to epitopes
  - Tools
    - Epitope Conservancy
    - Direct linking
  - Direct links to pathogen specific information
  - Point out literature missed



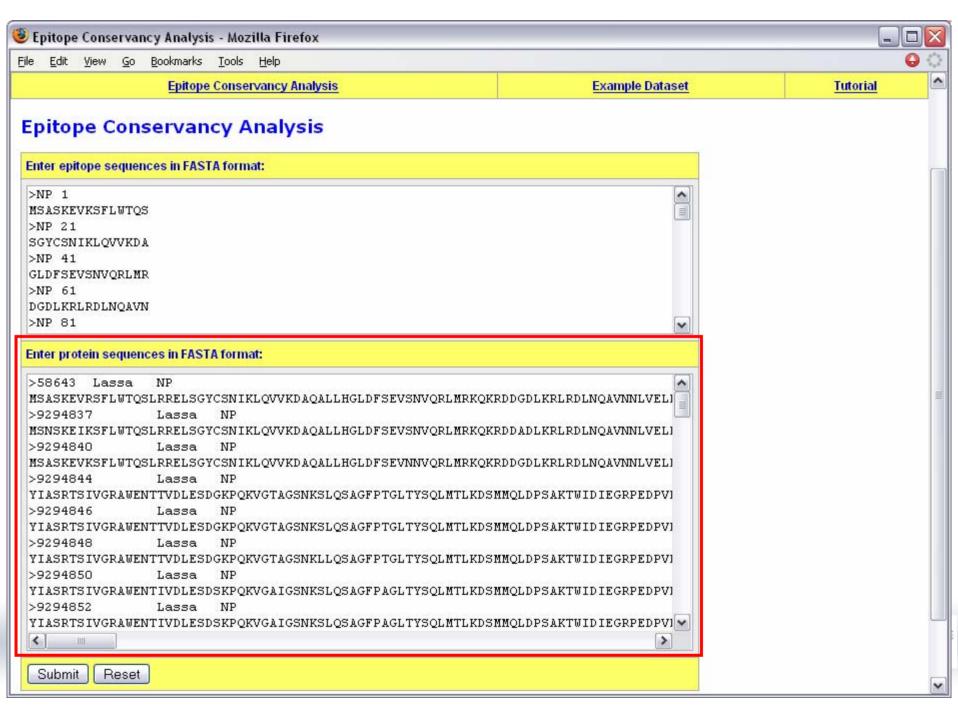
# Assigning Epitope Sources

- Literature: "... Epitope SLRTYKWQL comprising residues 46-54 of the influenza matrix protein..."
- Problem: We often want sequence of source protein
- Process: assign a SwissProt / GenBank protein that:
  - contains epitope (position match if possible)
  - matches source species (strain if possible)
  - matches name
- Better: Non-redundant set of high quality sequences with pathogen specific consistent naming conventions



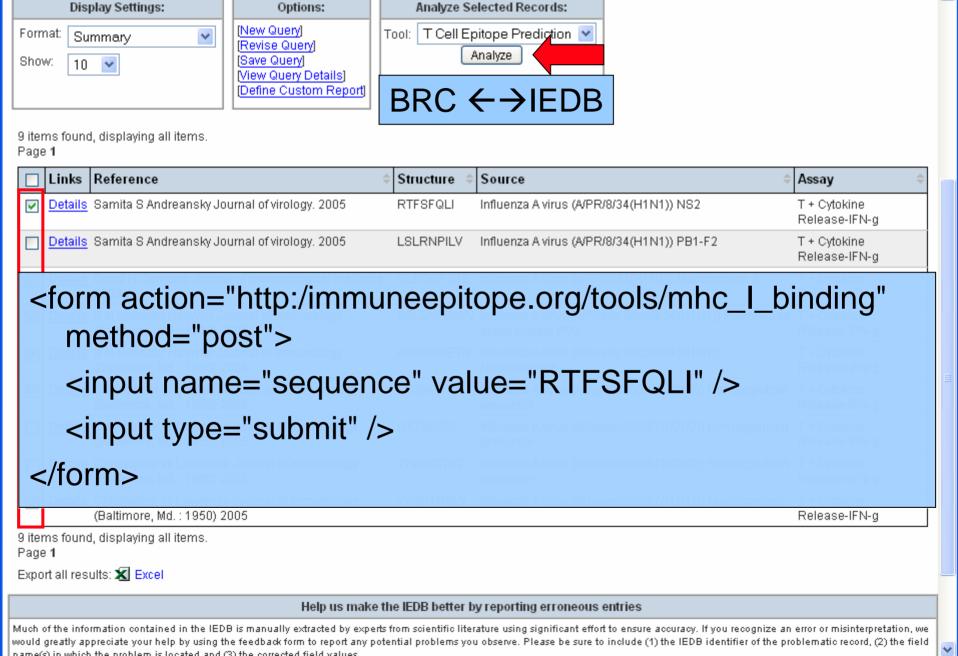
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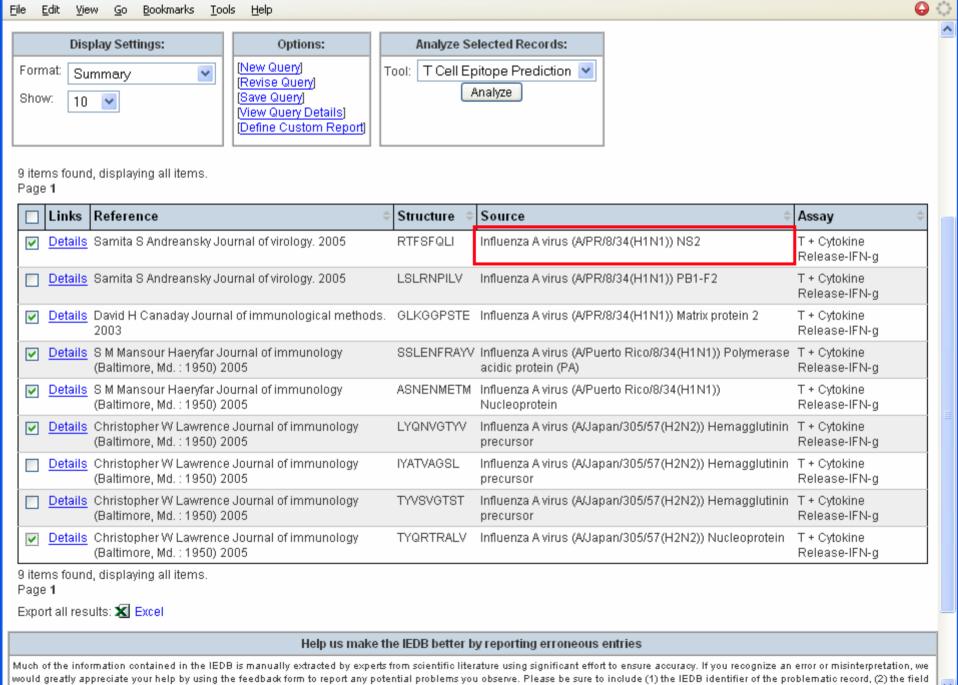
🤎 Immune Epitope Database and Analysis Resource - Mozilla Firefox

Tools

Bookmarks

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🐸 Immune Epitope Database and Analysis Resource - Mozilla Firefox

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